REMARKS

Claims 1-5, 8-10 and 16-18 are pending in the present application. Claims 1-5, 8-10 and 16-18 stand rejected. By this response, claim 1 has been amended. No new matter is added. Reconsideration is respectfully requested in light of the above amendments and following arguments. Accordingly, claims 1-5, 8-10 and 16-18 are currently under consideration.

Claim Amendment Support

Support for the amendments to claim 1 can be found throughout the specification, for example, at page 10, line 15 – page 11, line 2, page 33, lines 3-4, and Example 2, Table 2.

Claim 1 has been amended without prejudice or disclaimer of any previously claimed subject matter. The amendment is made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. Additionally, amendment of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 1-5, 8-10 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully traverses.

I. The Examiner alleges that none of the working examples "evidence[] that the administration of an oligonucleotide comprising the CpG motif suppresses RSV infection in a subject that has been exposed to RSV." *See* Office Action, at page 4. In response, claim 1 has been amended to recite a "method of suppressing a respiratory syncytial virus (RSV) infection in an individual *who is at risk of being exposed to RSV*, comprising administering a composition to the respiratory tract of said individual by local administration, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to

suppress an RSV infection" (emphasis added). The amendment is made solely to expedite prosecution without prejudice or disclaimer of any previously claimed subject matter. The newly amended claim 1 is enabled by the specification and in particular Example 2, Table 2, Group 2, where local administration of ISS prior to RSV infection is shown to be effective at reducing RSV titer. Therefore, Applicant requests that this ground for rejection be withdrawn.

The Examiner alleges on page 5 of the Office Action that "Example 2 provides that the administration of an oligonucleotide comprising the CpG motif does not suppresses [sic] RSV infection...." In support, the Examiner states that "[t]he data set forth in Table 1 clearly evidences that the administration of an oligonucleotide comprising the CpG motif does not suppress RSV infectivity in a subject, even when the oligonucleotide is administered prior to RSV infectivity." See page 5 of the Office Action.

Applicant respectfully submits that the Examiner's characterization of the specification is in error. Applicant notes that Table 1 is a summary of the protocol used for testing the ability of local administration of ISS to reduce RSV viral titer and does not show any actual results. See page 39, line 23; see also page 40 (the title of Table 1 is "Protocol"). Table 1 indicates, among other items, the dose of ISS given, the day ISS was given, the day RSV was given, the day of harvesting tissue, and the end-point *to be accessed* in the experiment. See page 40, Table 1. The "End-point" according to Table 1, column 7 when read in conjunction with the text of example 2 (in particular at page 39, lines 21-23) would be understood by one skilled in the art to mean that the end-point to be accessed in the experimental protocol is the level of RSV in the lung tissue. Thus, contrary to the Examiner's allegation, Table 1 merely lays out a protocol for the experiment and provides no evidence whether the CpG motif does or does not suppress RSV infectivity in a subject.

The Examiner, however, further alleges that Example 3 is contrary to Example 2 and "provides that the administration of an oligonucleotide comprising the CpG motif was not effective at reducing viral titers...." See Office Action page 5-6. Example 2 demonstrates that in an art-accepted model of a respiratory virus, namely cotton rat infected with respiratory syncytial virus (RSV), ISS is effective at reducing viral titers especially if administered *locally* (*i.e.*, at a site of infection) and before viral infection. Example 3 is directed to *non-local* administration on the other

hand and thus provides no contrary conclusion. The Applicant notes that claim 1, as amended, recites "administering a composition to the respiratory tract of said individual by *local* administration" (emphasis added). The amendment is made solely to expedite prosecution without prejudice or disclaimer of any previously claimed subject matter. Applicant submits that claim 1, as amended, is enabled and request withdrawal of this ground for rejection.

II. The Examiner alleges that undue experimentation is required of the skilled artisan to practice the invention. Applicant respectfully traverses. The claims, as amended, are directed to a "method of suppressing a respiratory syncytial virus (RSV) infection in an individual who is at risk of being exposed to RSV, comprising administering a composition to the respiratory tract of said individual by local administration, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, ... and wherein said composition is administered in an amount sufficient to suppress an RSV infection."

The specification teaches structural and sequence characteristics of an ISS comprising the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length. The specification states that "ISS have been described in the art and *may be readily identified using standard assays* which indicate various aspects of the immune response, such as cytokine secretion, antibody production, NK cell activation and T cell proliferation." Page 17, lines 3-10, emphasis added. The specification provides a number of references that describe ISS. See pages 3-4.

On page 17, lines 11-15, the specification teaches that "[t]he ISS can be of any length greater than 6 bases or base pairs and generally comprises the sequence 5'-cytosine, guanine-3', preferably greater than 15 bases or base pairs, more preferably greater than 20 bases or base pairs in length." The specification teaches that an ISS may also comprise the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3'. See page 17, line 15-16. The specification teaches that an ISS may also comprise the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, C-3'. See page 17, line 16-17. The specification teaches that an ISS may comprise (*i.e.*, contain one or more of) the

sequence 5'-T, C, G-3'. See page 17, line 17-19. The specification also teaches that in some embodiments, an ISS may comprise the sequence 5'-C, G, pyrimidine, pyrimidine, C, G-3' (such as 5'-CGTTCG-3'). See page 17, line 19-20. The specification also teaches that in some embodiments, an ISS may comprise the sequence 5'-C, G, pyrimidine, pyrimidine, C, G, purine, purine-3'. See page 17, line 20-22. The specification also teaches that in some embodiments, an ISS comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine-3' (such as 5'-AACGTT-3'). See page 17, line 22-23. The specification also teaches that in some embodiments, an ISS may comprise the sequence 5'-purine, T, C, G, pyrimidine, pyrimidine-3'. See page 17, line 24-25. Furthermore, the specification teaches approximately 160 specific ISSs. See page 18, line 9 through page 20, lines 2.

Further, the specification teaches an assay to determine whether an ISS is administered in an amount sufficient to suppress an RSV infection. The specification discloses several methods for assessing suppression of RSV infection. The specification teaches that "[r]hinitis, nasal mucous production, severity of cough, myalgia, elevated body temperature, and other symptoms of respiratory virus infection may be easily measured using simple tests and/or scales as are known in the art. Viral titer may be assessed in biological samples using standard methods known in the art." Page 35, lines 10-15. In addition, Example 2 teaches that administration of an immunostimulatory sequence (ISS) to an individual "before infection ... was effective at reducing viral titers." See page 40, lines 9-10.

Based on the teaching of the specification, a person of ordinary skill in the art would be able to practice the claimed invention without undue experimentation.

The Examiner at page 6 further states that the application has shown that the administration of an illustrative ISS, that is, the ISS shown in SEQ ID NO:1, was the only sequence used in working examples. The Examiner at page 12 additionally states that the application does not offer guidance in the specification concerning the effective use of oligonuclotides containing CpG motif to suppress RSV infection in an individual. Applicant respectfully traverses.

First, a specific level of suppression of an RSV infection, or clinical efficacy sufficient to suppress an RSV infection, is not required for compliance with the enablement requirement of

Section 112, first paragraph, as relates to the claims. The presently amended claims merely require that the "composition is administered in an amount sufficient to suppress an RSV infection."

Second, SEQ ID NO:1, which was used in Example 2 is comprised of the sequence recited in Claim 1, that is 5'-C,G -3' (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); comprises the sequence recited in Claim 2, that is 5'-T, C, G-3' (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); comprises one of the sequences recited in claim 3, that is 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3' or 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, C-3 (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); comprises the sequence recited in Claim 4, that is 5'-AACGTTCC-3', 5'-AACGTTCG-3', 5'-GACGTTCC-3', and 5'-GACGTTCG-3 (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); and comprises the sequence recited in claim 5, that is 5'-TGACTGTGAACGTTCGAGATGA-3' (SEQ ID NO:1). In fact, the specification demonstrates that a sequence comprising the ISS recited in claim 1, 2, and 5 and one of the ISS sequences recited in claim 3 and claim 4 is effective in the animal models disclosed in the Examples.

The Examiner references Infante-Durante et al. as teaching the need for a balance between Th1 and Th2 type immune responses. The Examiner also references Aoki et al., Bohn et al., Sakao et al., Zaitseva et al., and Masihi, K. as teaching that Th1 associated cytokines have different levels of efficacy against intracellular pathogens (none of which include RSV). The Examiner further states that Krieg et al. and Mutwiri et al. teach that the Th1 associated cytokine profiles for oligonucleotides vary from one oligonucleotide and species of subject to the next and that Yamamoto et al., Equils et al., Agrawal et al., and Olbrich et al. evidence the challenges in harnessing the immunostimulatory activity of oligonucleotides containing the CpG motif to trigger an innate immune response. Compliance with Section 112, first paragraph does not require optimizing ISS sequences. Whether or not different Th1 associated cytokines have different efficacy against intracellular pathogens or different ISS that have different activities in different mammals, the claimed invention is enabled if one of skill in the art can make and use the claimed invention based on the disclosure in the specification coupled with knowledge known in the art, without resorting to undue experimentation.

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As the court held in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988), the test for enablement does not rest merely on the quantity of experimentation that would be required to practice an invention, "since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Contrary to the Examiner's assertion, the quantity of experimentation is not a criteria for undue experimentation. Applicant submits that the disclosure of specific ISS sequences that "comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length," wherein the ISS "is administered in an amount sufficient to suppress an RSV infection," disclosure of methods for assessing suppression of RSV, and examples of suppression of RSV when the ISS are locally administered to the respiratory tract of an individual at risk of being exposed to RSV, enable one of skill in the art to make and use the claimed invention without resorting to undue experimentation.

If the rejection is maintained, Applicant requests the Examiner to provide an affidavit under 37 C.F.R. 1.104(d)(2) stating facts within the knowledge of the Examiner as to why the rejection should be maintained. Applicant reserves to right to explain or contradict the assertion with their own affidavits.

Therefore, Applicant submits that claims 1-5, 8-10 and 16-17 enabled in accordance with 35 U.S.C. § 112, first paragraph and request withdrawal of this ground for rejection.

Double Patenting

Claims 1-5, 8-10 and 16-17 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 11 of copending Application No. 10/898,512. When the conflicting claims have been found to be allowable, Applicant will address this provisional double patenting rejection with a terminal disclaimer.

Claims 1-5, 8-10 and 16-17 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10/426,237. When the conflicting claims have been found to be allowable, Applicant will address this provisional double patenting rejection with a terminal disclaimer.

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CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and allow this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882000900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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